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Risk factors for poor outcomes and therapeutic strategies for seasonal and pandemic influenza

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Abstract. Seasonal influenza is a leading cause of morbidity and mortality worldwide annually while pandemic influenza, a unique entity, poses distinct challenges. The pediatric population is the primary vector for epidemics and the main focus of this article. While primary prevention with universal influenza vaccination is the best protection against significant illness, the antigenic shift and drift unique to influenza viruses leave a large population at risk even with universal vaccination. Early in an epidemic various diagnostic tests are available and discussed here. However, once an epidemic is established, testing is no longer necessary for diagnosis. Groups with particular vulnerability to serious illness include those <6 mo of age, children with underlying neuromuscular disease, pulmonary disorders, or other comorbid conditions. Early treatment with neuraminidase inhibitors is recommended for those with influenza infection requiring hospitalization. Respiratory failure and need for mechanical ventilation are the leading indications for intensive care unit admission among children. Complications of influenza such as pneumonia, empyema, myocarditis and neurologic involvement increase risk for intensive care unit admission and will be discussed as will the use of extracorporeal membrane support. An overview of the epidemiology of influenza with an emphasis on risk factors for critical illness and poor patient outcomes in the pediatric population as well as treatment strategies for critically ill children will be presented. Additionally, we will address some of the unique challenges posed by pandemic influenza and mitigation strategies.

Keywords: Critical illness, influenza, pandemic, surge capacity

1. Introduction

Each year seasonal influenza epidemics are responsible for significant increases in clinic visits and hospitalizations at great cost to healthcare [1–5]. Influenza pandemics have likely plagued humans for centuries, with the most recent being the 2009 H1N1 influenza pandemic (pH1N1). Along with the challenges in caring for critically ill pediatric patients with seasonal influenza, the threat of the next influenza pandemic has further added new challenges to pediatric critical care. In this review, we will provide an overview of the epidemiology of influenza with an emphasis on risk factors for critical illness, treatment strategies for

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critically ill pediatric patients, as well as patient outcomes. In addition, we will outline differences between seasonal and pandemic influenza as well as mitigation strategies.

2. Virology

Influenza virus is a ribonucleic acid (RNA) virus and a member of the orthomyxoviridae group of viruses. There are three influenza types: A, B, and C. These types are distinguished on the basis of their internal nucleoprotein and matrix proteins, which are specific for each viral type. Influenza A viruses infect a range of animal species, including horses, swine, birds, seals and humans. Influenza B viruses infect only humans, while influenza C virus infects humans and swine. Influenza A viruses are further categorized into subtypes that are determined by the antigenicity of the surface hemagglutinin (H) and neuraminidase (N). Thus far a total of 16 distinct hemagglutinin and 9 neuraminidase influenza A subtypes have been identified. Historically, influenza A human infections have been caused by three subtypes of hemagglutinin (H1, H2 and H3) and two neuraminidase subtypes (N1 and N2); more recently human infections by the previously avian-restricted subtypes H5, H7 and H9 have been reported [6].

3. Seasonality and transmission

Under selective pressure, small mutations in the hemagglutinin and neuraminidase genes result in antigenic drift. Antigenic drift allows for evasion of host immune systems, and is responsible for seasonal epidemics [7]. In temperate regions, seasonal influenza infections peak during fall and winter months. In tropical regions, seasonal influenza occurs throughout the year but increases during rainy seasons. This pattern of seasonality is further increased by the close proximity to others during colder months [7, 8]. Frequently, during seasonal influenza, there is co-circulation of both influenza A and B in the community. Seasonal outbreaks tend to follow a predictable pattern; children are infected early in epidemics, followed by adults [8, 9]. Stockmann et al. [10] demonstrated seasonal influenza infections peak first in older school age children (12–18 yr) who may be more likely to spread the virus due to their wide contact networks. Furthermore, adolescents have low immunization rates [11]. Influenza virus can be detected in respiratory secretions 24 hr prior to symptom onset. Viral shedding peaks at three days and resolves within seven days in adults, however among young children shedding may be prolonged, which may contribute to transmission [7, 12].

4. Burden of influenza hospitalizations and mortality

The World Health Organization estimates that seasonal influenza results in approximately 1 billion cases of influenza, 3–5 million cases of severe illnesses and 300,000–500,000 deaths annually worldwide [13]. Globally, 5–10% of adults and 20–30% of children are infected annually [14]. In the United States, 5–20% of the population and an estimated 10–40% of children are infected with influenza annually [12, 15, 16]. The Centers for Disease Control and Prevention (CDC) estimate that nearly 300,000 hospitalizations among adults and children due to influenza occur annually [15]. Influenza-related hospitalization rates are similar among young children (<5 yr) and adults (50–64 yr) [15]. The CDC estimate more than 20,000 influenza-related hospitalizations occur annually in the United States in children less than 5 yr of age, with rates highest among those less than 6-month-old [15, 17]. The majority of seasonal influenza-related deaths occur in adults aged 65 yr and older [18]. In contrast, influenza-related deaths in children younger than 19 yr, is low (<1% of influenza-related deaths) [18]. Among children, most deaths occur in children <5 yr and the highest mortality rate is among children <6 mo [19].

Pandemic influenza outbreaks are caused by influenza A. Pandemic influenza strains arise from antigenic shifts, major changes in the hemagglutinin or neuraminidase genes, and are distinct entities both clinically and epidemiologically from seasonal influenza [20]. The antigenic shift leads to an immunologically naïve population being exposed to a "new" virus. It tends to disproportionately target the young and healthy compared to seasonal influenza and leads to increased morbidity and mortality in this population. Thus far, there have been four pandemics in the last 100 yr, all of which have been associated with significant morbidity and mortality worldwide [21, 22] (Table 1).

Table 1
Previous influenza pandemics and associated mortality

Pandemic	USA deaths	Worldwide deaths
1918-1919 "Spanish flu"	650,000	50,000,000
1957–1958 "Asian flu"	70,000	1,000,000
1968-1969 "Hong Kong flu"	34,000	700,000
2009-2010 H1N1	8,870–18,300	151,700–575,400

5. Viral testing

Appropriate treatment of patients with influenza depends on accurate and timely clinical and laboratory diagnosis. The laboratory-confirmation of influenza infection in the presence of clinical symptoms guides use of antiviral therapy and reduces ancillary medical testing and inappropriate use of antibiotics [23]. However, because bacterial infections can produce symptoms similar to influenza, bacterial infections should be considered and appropriately treated, if suspected.

Diagnostic tests available for the detection of influenza virus include rapid antigen testing, immunofluorescence assays, viral culture and real time reverse transcription polymerase chain reaction (RT-PCR) testing (Table 2). Preferred samples for influenza testing include nasopharyngeal or nasal swab samples and bronchial or endotracheal aspirate samples. Samples collected within the first five days of illness have the highest yield for testing. The sensitivity and specificity of the various influenza diagnostic tests vary by diagnostic test, type of respiratory specimen, and the laboratory that performs the test. Rapid antigen testing and immunofluorescence have lower sensitivity and specificity compared to viral cultures and molecular-based assays. Therefore, providers should consider confirming negative tests with more sensitive assays, especially during periods of peak influenza activity. False-positive rapid test results are likely to occur during periods of low influenza prevalence. A positive RT-PCR and other molecular assay indicate either confirmation of influenza virus infection or RNA from non-viable influenza virus. A test may also be positive for a person who has recently (within 7 days) received the intranasal administration of live attenuated influenza virus vaccine. Otherwise, false positives rarely occur. A negative RT-PCR result suggests no evidence of influenza viral RNA or improper sample collection if influenza is still clinically suspected. The traditional viral culture method can take up to 3 to 10 days for identification of influenza and therefore are not readily available for clinical decision-making. The ideal test would have the fast turnaround time and simplicity of a rapid antigen test, with high sensitivity and specificity. Isothermal nucleic acid amplification can provide results within 15 min and has improved sensitivity over rapid antigen testing [24, 25]. This may be a reasonable option for hospitals that do not offer rapid antigen testing.

As with any diagnostic test, results should be evaluated in the context of clinical and epidemiologic information available to providers. In the presence of clinical signs and symptoms of influenza, a clinical diagnosis of influenza can be made without testing during influenza season and if it is known that the influenza has reached a community.

6. Antiviral therapy

Influenza antiviral treatment is recommended for all persons with suspected or confirmed influenza requiring hospitalization or who have progressive, severe or complicated illness regardless of previous health or vaccination status. Neuraminidase inhibitors (oseltamivir and zanamivir) have activity against both A and B strains, and are the drugs of choice for influenza treatment and chemoprophylaxis [7]. Oseltamivir is available as an oral formulation, while zanamivir is available in intravenous and inhaled formulations. Despite the widespread use of oseltamivir, oseltamivir-resistant viruses are rare (<1%) [26]. Resistance to zanamivir is even less common [26]. Surveillance for resistant strains is ongoing. The adamantanes (amantadine and rimantidine), are no longer recommended for the treatment of influenza A infection because of near universal resistance [7].

Early initiation of anti-influenza therapy is recommended for all hospitalized patients to decrease the risk of influenza-related complications. In a prospective study in which 71% of adults began treatment >48 hr after illness onset, oseltamivir treatment was associated with decreased risk of death within 15 days of hospitalization (Odds ratio [OR], 0.2; 95% confidence interval 8CI], 0.06–0.8). However there was no difference in 30-day mortality (OR, 0.41; 95% CI, 0.14–1.2) [27]. A Thailand study of 445 hospitalized adults and children with laboratory-confirmed influenza infection, also found a reduced odds of death among those treated with oseltamivir (OR, 0.13 adjusted for age; 95% CI, 0.04–0.4) [28]. Studies that included

Table 2
Influenza testing methods

Method	Influenza types detected	Preferred specimens	Test time
Rapid influenza diagnostic tests	A and B	Nasopharyngeal swab, (throat swab), nasal wash, nasal aspirate	<30 min
Immunofluorescence (direct fluorescent antibody staining)	A and B	Nasopharyngeal swab, nasopharyngeal or bronchial wash, nasal or endotracheal aspirate	2–4 hr
Viral cell culture	A and B	Nasopharyngeal swab, nasopharyngeal or bronchial wash, nasal or endotracheal aspirate	3–10 days
Rapid cell culture (shell vials)	A and B	As above	1–3 days
Reverse transcription polymerase chain reaction (singleplex and multiplex) and other molecular assays	A and B	Nasopharyngeal swab, throat swab, nasopharyngeal or bronchial wash, nasal or endotracheal aspirate, sputum	2–4 hr
Isothermal nucleic acid amplification	A and B	Nasopharyngeal swab	<15 min

hospitalized patients treated both less than and greater than 48 hr after illness onset, demonstrated benefit in both groups but greater benefit in those treated within 48 hr [29–31].

The American Academy of Pediatrics (AAP) Committee on Infectious Disease recommends treatment should be offered to any child hospitalized with severe, complicated or progressive illness attributable to presumed or confirmed influenza. This treatment should be offered regardless of influenza immunization status and/or even if illness began >48 hr before admission. Individuals at high risk of influenza complications should also receive antiviral treatment [26] (Table 3).

7. Risk for intensive care admission

Influenza-related complications are associated with significant morbidity and mortality. Up to 15% of hospitalized children with seasonal or pandemic, e.g. pH1N1, influenza require intensive care unit (ICU) care [3, 32, 33]. Respiratory failure is the most common indication for ICU care among children with influenza. Approximately 50% of children requiring ICU care for influenza require mechanical ventilation [33]. Less common influenza-related complications such as lung abscess, empyema, tracheitis, encephalopathy, myocarditis, acute renal failure, sepsis and bacteremia (4% collectively of hospitalized children with influenza) are also risk factors for requiring ICU admission [32]. The most common underlying medical conditions among those admitted to the ICU with seasonal influenza or pH1N1 are neurologic conditions (20–30%) [33–35]. Children with neurologic or neuromuscular conditions are also more likely to have influenza-related severe complications (Relative risk (RR) 4.0, 95% CI 1.9–8.2), of which pneumonia is the most common followed by respiratory failure [36]. A study of children admitted to the ICU in Australia and New Zealand reported risk factors for severe influenza, defined as death or ICU stay >7 days, include those presenting with septic shock, after cardiac arrest or with one or more comorbidity [35].

Table 3
Influenza antiviral treatment recommendation summary*

Antiviral treatment is recommend for any patient with confirmed or suspected influenza who:
Is hospitalized Has severe, complicated, or progressive illness Or, is at high risk for influenza related complications
Individuals at higher risk of influenza complications recommended for antiviral treatment:
Children <2 yr** Adults $\geq$65 yr Individuals with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematologic (including sickle cell disease), metabolic disorders (including diabetes mellitus), or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy, stroke, intellectual disability, moderate to severe developmental delay, muscular dystrophy, or spinal cord injury) Individuals with immunosuppression, including that caused by medications or by human immunodeficiency virus infection Pregnant women or postpartum (within 2 wk of delivery) Children $\leq$18 yr who are receiving long-term aspirin therapy American Indians/Alaska natives Individuals with morbid obesity (i.e. body mass index $\geq$40) Residents of nursing homes or other chronic-care facilities

*Adopted from Centers for Disease Control and Prevention and American Academy of Pediatrics [26, 70]. **The Centers for Disease Control and Prevention describes children <5 yr of age as being at higher risk of influenza complications. However, the risk is highest for those aged <2 yr.

7.1. Respiratory failure

Severe upper and lower respiratory tract infection with influenza can cause respiratory failure in adults and children. It is estimated that up to 9% of hospitalized children with influenza require mechanical ventilation [36, 37]. Factors that increase the risk of influenza-related respiratory failure are cardiovascular disease, neurological or neuromuscular disease, non-asthma chronic lung disease, metabolic disease, hepatic disease, bacterial pneumonia, age 2–11 mo and lack of influenza immunization [37, 38]. Treatment with neuraminidase inhibitors decreases the need for mechanical ventilation in children hospitalized with influenza, especially if administered before the third hospital day [37].

7.2. Extracorporeal membrane oxygenation

Extracorporeal membrane oxygenation (ECMO) is a potentially life saving modality in children with influenza. Among children admitted to the ICU with seasonal influenza or pH1N1, 2–4% receive ECMO [33, 34]. Among pediatric patients with influenza who receive ECMO, 57% survive [39]. Risk factors for higher mortality in children receiving ECMO for respiratory failure include pre-existing underlying medical conditions, pre-ECMO duration of mechanical ventilation >13 days, and multi-organ failure [39]. A meta-analysis of young adults requiring ECMO during the 2009 H1N1 pandemic found the majority of patients were treated with veno-venous ECMO (94%), required ECMO within 2 days of hospitalization and required ECMO for a median of 10 days. The mortality in the reviewed studies ranged from 8%–65%, however mortality was <30% in six of the eight studies [40]. Veno-venous ECMO appears to be a reasonable treatment option in young, otherwise mostly healthy people with severe hypoxic respiratory failure from influenza.

7.3. Secondary bacterial infections

The relationship between influenza and secondary bacterial infection resulting in severe illness and death has been well documented. Many *in vitro* and animal studies have provided clues to the potentially lethal synergism between influenza virus and subsequent bacterial infections. Increased adherence of *Streptococcus pneumoniae and Staphylococcus aureus* to cultured cells has been reported after pre-infection of culture cells with influenza virus [41]. In addition, recent studies suggest a strong correlation between invasive pneumococcal disease 2 to 4 wk after influenza virus infection [42, 43]. It is of interest that this seems to corroborate historical data on the 1918 influenza pandemic, in which many deaths resulted from pneumonia associated with S. pneumoniae, with a peak mortality rate 14 days after the onset of symptoms [44, 45]. More recently, bacterial co-infections are identified in almost 25% of seasonal influenza-related deaths among children [19]. During the 2009 pandemic, 43% of influenza-related deaths among children in the United States had a bacterial co-infection [46].

Bacteria most commonly isolated from children with influenza include *S. pneumoniae, S. aureus, Streptococcus pyogenes* and *Heamophilus influenzae* [19]. During previous pandemics, *S. pneumoniae* and *S. aureus* were frequently isolated from adults and children with pneumonia [47]. During the 2003-2004 influenza season in the United States, *S. aureus*, especially methicillin resistant strains (>50%), was the most commonly isolated organism among influenza-related deaths with a bacterial co-infection [19]. During the 2009 H1N1 pandemic, the organisms isolated after death differed among adults and children; *S. aureus* most commonly from children, and *S. pneumoniae* from adults [48].

Secondary bacterial pneumonia is a common complication of influenza. The reported prevalence of bacterial pneumonia with influenza has been variable because of different definitions of pneumonia used in the various studies. Among 20,000 hospitalized children with influenza from 2006–2009, international classification of diseases, ninth revision (ICD-9) coded bacterial pneumonia was reported more frequently in children with pH1N1 compared to seasonal influenza (8.4% versus 5.6% respectively, $P < 0.001$) [37]. In another study conducted during the same time period, radiographic pneumonia was reported in 23% of hospitalized children with seasonal influenza or pH1N1 [49].

Bacterial pneumonia complicated by empyema develops in a small proportion of children, with increased number of cases reported during circulation of influenza and other respiratory viruses. Empyema was commonly reported during the 1918 influenza pandemic [47]. Similarly, during the 2009 H1N1 pandemic, hospitalization for parapneumonic empyema among children increased, of which *S. pneumoniae* was identified in up to 66%. [50, 51].

If secondary bacterial pneumonia is identified or suspected, antibiotics should be administered promptly. Similar organisms are implicated in secondary bacterial pneumonia and community-acquired pneumonia. Therefore, antibiotic selection can be based on community-acquired pneumonia treatment guidelines [52]. For severely ill children with influenza-related bacterial pneumonia, clinicians should consider addition of antimicrobials with activity against methicillin-resistant *S. aureus*.

7.4. Myocarditis

Acute myocarditis was commonly reported and often fatal in earlier influenza pandemics. During the 1918 and 1957 pandemics, myocarditis was reported in 30–50% of fatal influenza cases [53, 54]. With the more recent 2009 influenza pandemic, Randolph et al. [34] reported myocarditis in 1.4% of critically ill children with influenza. Similarly, low rates (0.4%) of myocarditis were reported among children with seasonal influenza in Canada [55]. However, Guarner et al. [56] reported histopathologic evidence of myocarditis in 30% of children with an influenza-related death, suggesting myocarditis may be more common in critically ill patients with influenza than previously thought. Ukimura et al. [57] reviewed 58 cases of myocarditis associated with pH1N1, of which 14 cases (24%) were <17 yr of age. In this review, clinical signs and symptoms of chest pain or worsening dyspnea were associated with development of myocarditis during the first few days of illness in about half of the patients [57]. Due to the potential for rapid progression, early diagnoses and treatment is necessary. Electrocardiography and echocardiography are useful and sensitive tests for myocarditis. Treatment with neuraminidase inhibitors is crucial in the treatment of influenza-related myocarditis to eliminate the infection but it is unclear if it significantly improves survival [57]. Cardiovascular support may be necessary via left-ventricular assist device or ECMO. Ukimura et al. [57] reported a survival rate of 76% (13 of 17) among individuals supported with mechanical circulatory support for influenza-related myocarditis.

7.5. Neurologic complications

Neurologic complications associated with influenza are more common than myocarditis, however are still rare. Approximately 8% of hospitalized children with seasonal influenza or pH1N1 have an influenza-related neurologic complication (INC) [58–60]. In a retrospective cohort of hospitalized children with influenza in the US, the incidence of INC was four cases per 100,000 person/yr [59]. The most common INCs are seizures, including febrile seizures, and encephalopathy [58, 59]. Seizures account for 50–90% of INCs [58–60]. Other less commonly reported INCs include stroke, aseptic meningitis, Guillain-Barré syndrome, Reye's syndrome, transverse myelitis, myasthenic crisis, and coma [58, 59]. INCs are more likely to occur in individuals with neurologic or neuromuscular diseases (OR, 5.6 adjusted for age; 95% CI, 3.2–9.6) [59]. An age of 6 mo to 4 yr is also an independent risk factor for INC, with those aged 2–4 yr at the highest risk [59].

The outcome following INCs ranges from complete recovery to death. In a study with 72 US children with an INC, Newland et al. [59] reported all survived and only one child had permanent neurologic sequelae. In a study of 103 children with INC, Muhammad et al. [60] reported four (3.8%) died and three (2.9%) had persistent neurologic sequelae. In contrast, the morbidity and mortality associated with INC are higher in Japan. Between 1998 and 2002, 22% of children with influenza-associated encephalopathy died in Japan, which decreased to 8% between 2004 and 2010 [61, 62]. Interestingly, during the 2009 H1N1 pandemic in Japan, there was a significant increase in cases of influenza-associated encephalopathy, however the mortality among those with encephalopathy was much lower (3.6%) compared to preceding seasons [62]. However, encephalopathy remained a leading cause of death among children in Japan with pH1N1 [63].

8. Influenza and healthcare capacity

During influenza pandemics, children are disproportionately represented in the ICU population and tend to require mechanical ventilation more than adults, but have better survival [35]. While a study by Eriksson et al. [37] revealed pediatric patients with pH1N1 were less likely to require intubation and mechanical ventilation compared to those with seasonal influenza, they also identified a three-fold increase in hospitalizations among children with pH1N1 and overall increased use of mechanical ventilators. The ability to respond to an increase in demand, which exceeds the normal, is referred to as surge capacity. This includes things such as push-packs (pre-packed supplies held in reserve to meet increased demand), overflow of patients outside of typical care areas such as mechanically-ventilated patients in the post-anesthesia care unit in addition to the ICU, use of personnel typically assigned to other areas transferred to the ICU, and triage of both patient disposition and allocation of resources such as ventilators and neuraminidase inhibitors [20, 64]. Rapid acquisition of local clinical and epidemiologic data during an influenza pandemic, may help establish reliable early estimates of critical care resource utilization and thus whether contingency measures will be needed to accommodate the influx of patients [65].

The increase in patients leads to a strain on resources and it is conceivable that patient demands may eventually exceed available resources and create the need to alter the focus of care from the individual to the population. The Institute for Medicine (IOM) identified five key elements for crisis standards of care: (1) strong ethical grounding, (2) ongoing community and provider engagement and education, (3) legal protection for healthcare providers and institutions, (4) clear indicators and triggers for implementation, and (5) evidence based clinical processes and operations [66]. In keeping with the IOM's recommendations, identifying which patients are most likely to benefit from these scarce resources is imperative. This divides the patient population into three categories: those who will survive without significant morbidity without the intervention, those who will likely die or survive with significant morbidity despite the intervention, and those who will survive without significant morbidity with the intervention. Adult scoring systems such as the simple triage scoring system have been validated to help allocate these resources but none are currently available for children [67]. With a lack of universally available validated pediatric scoring systems for predicting mortality, it is imperative that individual institutions and regional crisis management teams develop tools for clinicians to triage pediatric resources as part of their crisis planning process.

In 2010, the European Society of Care Medicine Task Force released recommendations for intensive care unit preparedness during an influenza epidemic or disaster, which expanded on the IOM general recommendations: (a) Establishment of ICU overflow areas with adequate monitoring equipment, (b) A centralized body that is in charge of resource allocation, (c) A communication system between key areas should be established a priori, (d)Institutions should have a plan to be able to increase human resources with caregivers practicing within their usual scope of practice, (e) Stockpiles of essential medical equipment, pharmaceuticals and supplies should be collected, (f) Infection control practices should be in place to protect both patients and staff, (g) A legal protection plan for staff should be in place in the event patients either have artificial support withdrawn or not offered, (h) Objective, ethical, and transparent triage criteria should be established and ICU triage should be based on those most likely to benefit, (i) Protocols for safe performance of high-risk procedures should be established and staff should be educated regarding these protocols [68].

While not typically addressed in preparedness guidelines, it is likely a significant proportion of medical and ancillary staff may abandon their workplace during a pandemic in order to protect themselves and their families [69]. Therefore, institutions should consider establishing both educational campaigns and onsite support and facilities to care for staff and their families.

Pandemic influenza poses unique challenges in that the need for medical intervention may exceed the capacity of institutions. Additionally, younger healthier populations, including medical staff, may be disproportionately affected. Allocation of resources to those most likely to benefit is crucial. While there is no validated triage tool for pediatric patients in pandemic influenza, it is important that institutions have a regionally coordinated plan in place prior to a pandemic.

In conclusion, seasonal and pandemic influenza are responsible for substantial mortality and morbidity among children. Bacterial co-infections and respiratory failure are the most common complications among children with severe influenza illnesses. Children with underlying medical conditions, particularly neurologic conditions, are at greatest risk for complications and need for ICU care. Early identification of influenza infection and antiviral therapy reduces influenza-associated mortality and morbidity.

Pandemics pose additional clinical and ethical challenges in management of influenza due to an influx of patients and increased demand for critical care resources. In the event of a pandemic, contingency planning for increased resource demand is crucial. Pediatric intensivists should take part in surge capacity planning because children are disproportionately affected during pandemics and critical care resources, including personnel, are often the limiting factor.

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